

REMARKS

Preliminary Remarks:

Upon entry of this Amendment, claims 13, 14, and 44 to 49 will be pending of which claim 13 is independent. Claims 38 to 43 are cancelled without prejudice to, or disclaimer of, the underlying subject matter (claims 1 to 12 and 15 to 37 were previously cancelled). Claims 13, 14, and 44 to 49 are amended to a method for producing an evolved protein involved in methionine biosynthesis pathway and to better conform the claims to current U.S. practice. Support for the claim amendments may be found in the specification as filed. *See, for example*, page 14, lines 23 to 32; page 23, lines 15 to 24; and page 45, lines 20 to 23. Therefore, no new matter is added.

Applicants thank the Examiner for the withdrawal of the objection to claim 49; the withdrawal of the rejection of claims 13, 14 and 38 to 49 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 12 to 14 and 38 to 49 of co-pending U.S. Pat. Appl. No. 10/781499 (U.S. Pat. Appl. Pub. No. 2005/0054060); and the withdrawal of the rejection of claim 42 under 35 U.S.C. § 112, first paragraph.

This Amendment is accompanied by a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114.

Claim Objection:

Claim 42 was objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 41. Both claim 41 and claim 42 are cancelled rendering this objection moot. Accordingly, Applicants respectfully request withdrawal of the objection to the claims.

Claim Rejections:

Rejections under 35 U.S.C. § 103

Claims 13, 14, 38 to 41 and 43 to 49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Richaud *et al.* (*J. Biol. Chem.* **268**(36), 26827-26835, 1993) in view of Short *et al.* (U.S. Pat. Appl. Pub. No. 2005/0124010). Claims 38 to 41 and 43 are cancelled and Applicants respectfully traverse this rejection with respect to claims 13, 14, and 44 to 49.

As amended, claims 13, 14, and 44 to 49 are directed to a method for producing an evolved protein involved in methionine biosynthesis pathway wherein disrupting the *metE* gene

in a microorganism and culturing the modified microorganism on a minimal medium containing methylmercaptan, leads to the evolution of a protein involved in the methionine biosynthesis pathway and therefore the microorganism is able to grow on the minimal medium.

Richaud *et al.* teach that the disruption of the *metC* gene and the joint over-expression of the *metB* gene in *E. coli* strains, which are auxotrophic for diaminopimelate, leads to the ability of these strains to grow on minimal medium. Richaud *et al.* do not teach disruption of the *metE* gene nor culturing the modified microorganism obtained on a medium containing methylmercaptan.

Short *et al.* do not overcome the deficiencies of Richaud *et al.* Short *et al.* describe a method for identifying proteins by differential labeling of peptides, using a plurality of labeling reagents, fragmenting the polypeptide into peptide fragments, and separating the peptides by chromatography. *See*, Short *et al.*, claim 1. Moreover, Short *et al.* teach isolation of cells comprising newly engineered phenotype, stating that “any phenotype can be added or modified” and fully explaining that the phenotype is obtained *by directed genetic modification*, not by an evolution process. *See*, Short *et al.*, paragraphs [1060] to [1066], in particular paragraphs [1062] to [1063].

However, Short *et al.* do not teach disruption of the *metE* gene nor culturing the modified microorganism obtained on a medium containing methylmercaptan. Therefore, the combination of Richaud *et al.* with Short *et al.* does not result in the method claimed in claims 13, 14, and 44 to 49. Applicants respectfully submit that claims 13, 14, and 44 to 49 are not unpatentable under 35 U.S.C. § 103(a) over Richaud *et al.* in view of Short *et al.* and respectfully request withdrawal of this rejection.

CONCLUSION

In view of the amendments and remarks above, Applicants respectfully submit that this application is in condition for allowance and request favorable action thereon. The Examiner is invited to contact the undersigned if any additional information is required.

As this response is filed within the shortened statutory period for reply, Applicants believe that no fees, other than the fee for the RCE, are due. If any additional fees are required, they may be charged to Deposit Account No. 50-4254, referencing Attorney Docket No. 2912956-026000.

Respectfully submitted,

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